THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 13

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte KAREN K. BROWN, SHARON A. BRYANT, RICHARD C. STEWART AND RICHARD E. PARIZEK

Appeal No. 93-2810
Application 07/547,733[1]

ON BRIEF

Before SMITH, RONALD H., SMITH, WILLIAM F. and GRON, Administrative Patent Judges.

GRON, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 of an examiner's final rejections of Claims 2-6, all claims pending in this

[1] Application for patent filed July 3, 1990.

application. Claims 2-6 stand rejected under 35 U.S.C. § 103 over the combined disclosures of (1) Brown[2] and Farrow[3] and (2) Bergey[4] and Boyle[5]. All claims stand or fall with the patentability of representative Claim 6 (Appellants' Brief (Br), page 3). Claim 6 appears in the attached appendix.

Appellants' invention is a method of preparing a cell-free solution of an immunogenic M-like protein extractable from Streptococcus zooepidemicus (hereafter S. zoo) bacteria. The solution is useful for immunizing horses against S. zoo. The method comprises (a) growing S. zoo bacteria, (b) adding mutanolysin enzyme to the bacteria, (c) incubating the addition product, (d) further adding an anionic detergent to extract M-like protein, (e) removing unlysed cells and cell debris from the supernate, and (f) sterilizing the supernate solution.

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2 Brown, Karen K., et al., U.S. Patent No. 4,582,798, patented April 15, 1986.

3 Biolological Abstracts, Vol. 80, No. 3, Ref. No. 18743 (August 1, 1985), abstracting Farrow, J.A.E., et al., Syst. Appl. Microbiol., Vol. 5, No. 4, pages 483-493 (1984).

4 Bergey's Manual of Systematic Bacteriology, Vol. 2, Section 12. Gram-Positive Cocco., "Streptococcus," Sneath, Peter H.A., ed., Williams & Wilkins, Baltimore, MD., pages 1049-1050 and 1052-1053 (1986).

5 Boyle, Michael D.P., et al., U.S. Patent No. 4,977,082, patented December 11, 1990 (application filed November 9, 1988).

Based on the record before us, we hold that the examiner erred in concluding that appellants' claimed invention is unpatentable over the cited prior art. In our view, the combination of all the prior art cited in this case would not have led persons having ordinary skill in the art to treat S. zoo with mutanolysin and an anionic detergent with the requisite reasonable expectation that an immunogenic M or M-like protein would be extracted thereby. In re O'Farrell, 853 F.2d 894, 903-904, 7 USPQ2d 1673, 1680-1681 (Fed. Cir. 1988); In re Dow Chemical Co., 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988); and In re Rinehart, 531 F.2d 1048, 1051, 1054, 189 USPQ 143, 147, 148 (CCPA 1976).

Findings

We make the following findings:

1. But for treatment of Streptococcus equisimilis (hereafter S. equi), Brown describes procedural steps identical to that claimed by appellants for preparing a cell-free immunogenic M-like protein solution from S. zoo, i.e., Brown treats S. equi with mutanolysin, extracts immunogenic M-like protein from the product with anionic detergent, and separates and sterilizes the M-like protein.

2. Brown clearly does not describe extraction of immunogenic M protein. Brown describes extraction of an "M-like" protein. Brown states (Brown, col. 1, lines 61-64):

> As used herein, the expression "M-like protein" means the immunogenic protein(s) of the Strep. equi organism which appears similar in molecular weight and activity to the M-protein of group A streptococci.

3. Brown teaches that mutanolysin is thought to act on linear sequences of N-acetylglucosamines and N-muramic acid residues. Brown states (Brown, col. 3, lines 7-10):

> Mutanolysin and other bacteriolytic enzymes (glycosidases) such as egg white lysozyme are thought to act on linear sequences of N-acetylglucosamines and N-acetyl-muramic acid residues of the bacterial cell walls.

4. Farrow appears to have examined the taxonomic relationships of various species of streptococci "using DNA-DNA hybridization, DNA base composition and biochemical tests."[6] Farrow apparently found that S. equi and S. zoo are closely related on the basis of DNA-DNA hybridizations:

> . . . S. equisimilis and streptococci of Lancefield serological groups C, G and L are a single species. S. equi and S. zooepidemicus were found to be closely related on the basis of DNA-DNA hybridizations. It

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[6] We express our disappointment at facing a deficient record. The abstract of Farrow's article is not the article itself. An article material to patentability is best considered in its entirety. The cost to appellants and the examiner of obtaining and considering the full text of the article during ex parte examination of a patent application is far less than the cost consequential to its consideration for the first time in a reissue or reexamination proceeding or in litigation contesting the validity of an issued patent since appellants at the first opportunity have greater latitude to respond to the prior art cited against and amend their claims. The resources of appellants and the PTO are best spent when patentability is considered at the earliest practical time of examination on the basis of the most complete statement of the prior art.

> is suggested that S. zooepidemicus be reclassified as S. equi ssp. **zooepidemicus** . . . .

5. The Farrow abstract teaches nothing about the comparative chemical sequences, the major chemical constituents, and the antigenic characteristics of proteins and polysaccharides in the cell walls. The close relationships Farrow found between S. equi and S. zoo do not appear to have been based on comparative biochemical or pathogenic test results.

6. Appellants and the examiner appear to agree that S. equi and S. zoo can be differentiated serotypically, i.e., S. equi has one serotype while S. zoo has fifteen different serotypes, structurally, and pathogenically (Br3-4; Examiner's Answer (Ans), pages 5-6).

7. Bergey teaches that the major chemical constituents of both S. equi antigens and other streptococci of Lancefield serological group C are N-acetylgalactosamine and rhamnose. According to Brown, however, mutanolysin acts on N-acetylglucosamines which Bergey teaches are major chemical constituents of M proteins of serological group A antigens (Bergey, Table 12.17, page 1049, S. pyrogens).[7] Bergey teaches that group A S. pyrogens, group C S. equi, and other streptococci of Lancefield serological group C

[7] We find no basis for and are confused by the examiner's statement that "Bergey further teaches the presence of certain M proteins in strains of Streptococcus belong to group C (Table 12.16, col. 3)" (Ans4, first full paragraph).

can all be differentiated by their biochemical characteristics (Bergey, Table 12.16, page 1049) even though the antigens of S. equi and the other group C streptococci clearly are all proteins and are all located in the cell walls (Bergey, Table 12.17, page 1049). With regard to serological group A streptococci, Bergey teaches that its M proteins "can be isolated by a number of procedures such as HCl extraction at pH 2.0, treatment with phage-associated lysin, mild pepsin digestion, treatment with detergents or other techniques, and can be further purified" (Bergey, page 1050, col. 1, first full paragraph).

8. Bergey suggests to persons skilled in the art that the biological differences between S. equi and S. zoo may not alone justify establishment of a separate species, i.e., "the strains are taxonomically referred to one taxon, namely group C" (Bergey, page 1053, col. 1, first full paragraph). The importance of the taxonomic grouping is minimized by Bergey's statement that the cellular and colonial morphology and the chemical structure of polysaccharides composed of N-acetylgalactosamines in the cell walls of S. equi and S. zoo of group C are very similar to that of S. pyrogens of group A (Bergey, page 1053, col. 1, second full paragraph).

9. In our view, the examiner clearly erred in finding that Boyle teaches "treating S. zooepidemicus with mutanolysin and detergent in a process to prepare an antigenic solution (col. 8,

lines 9-26)" (Ans3-4, bridging paragraph). Boyle states (Boyle, col. 8, lines 21-25; emphasis added):

> Bacterial pellets were extracted by a number of different methods, including treatment with the enzyme mutanolysin or heat extraction at neutral, acid or alkaline pH and in the presence of 2% SDS.

Boyle's Table 1 clarifies that 2% SDS detergent was employed in the heat extraction process only.

10. We find that Boyle's method of extracting Type VI IgG-Fc receptor from S. zoo either by treatment with mutanolysin or by heat treatment in the presence of 2% SDS does not describe or reasonably suggest appellants' claimed method. Nor can we determine based on this record whether Boyle's treatment of S. zoo with mutanolysin would have led persons having ordinary skill in the art to reasonably expect that S. zoo cell walls contain extractable immunogenic M-like proteins. More simply put, extraction of Type VI IgG-Fc receptor from the cell wall of S. zoo bacteria alone does not reasonably suggest that M-like proteins are present in and/or would inherently be extracted by mutanolysin treatment.

Discussion

Neither Brown, Farrow, Bergey nor Boyle expressly or inherently describe the multiple-step treatment of S. zoo required by appellants' claimed process. The examiner's finding that Boyle's process would inherently extract immunogenic M-like

protein from S. zoo because he extracted Type VI IgG-Fc receptor from the cell wall of S. zoo bacteria by treatment with mutanolysin and extraction with anionic detergent is, in our view, clearly erroneous. First, Boyle did not treat S. zoo with both mutanolysin and SDS. Second, Boyle did not extract, separate, or sterilize M-like proteins or acknowledge the presence of valuable immunogenic M-like proteins in the cell walls of S. zoo. Third, based on the combination of Bergey and Boyle, persons having ordinary skill in the art would have had no reason to expect that the cell walls of S. zoo contained valuable immunogenic M-like proteins.

Nor could persons having ordinary skill in the art reasonably have predicted from all the combined teachings of Brown, Farrow, Bergey and Boyle that mutanolysin acts on the cell walls of S. zoo to release antigens which are immunogenic M-like proteins, as is the case for S. equi (see Brown). That S. equi DNA are capable of hybridizing S. zoo DNA, that the two bacteria cannot be taxonomically differentiated based on DNA-DNA hybridizations, that the two bacteria have similar major chemical N-acetylgalactosamine and rhamnose constituents, and that their antigens are proteins found in the cell walls, do not alter the basic fact that the prior art differentiates S. equi from S. zoo serotypically, structurally, biochemically and pathogenically. In short, persons having ordinary skill in the art reasonably

would not have expected to be able to treat S. zoo with mutanolysin and extract immunogenic M-like proteins from the product with an anionic detergent.

We are mindful that obviousness under 35 U.S.C. § 103 does not require absolute predictability. In re O'Farrell, 853 F.2d at 903, 7 USPQ2d at 1681. However, here persons having ordinary skill in the art with all the prior art cited in this case before them reasonably could not have expected that Brown's process could be used successfully to extract immunogenic M-like proteins from S. zoo. Persons having ordinary skill in the art would not have had enough evidence to predict with any reasonable degree of assurance that the cell walls of S. zoo bacteria, like the cell wall of S. equi bacteria, were susceptible to mutanolysin activity and contained anionic detergent-extractable immunogenic M-like proteins. Absent such evidence, the method appellants claim would merely have been "obvious-to-try." In re Eli Lilly & Co., 902 F.2d 943, 945, 14 USPQ2d 1741, 1743 (Fed. Cir. 1990). To reject patentability under 35 U.S.C. § 103, more is required. We reverse.

Conclusion

1. The rejections of Claims 2-6 under 35 U.S.C. § 103 over the combined disclosures of Brown and Farrow are reversed.

2. The rejections of Claims 2-6 under 35 U.S.C. § 103 over the combined disclosures of Bergey and Boyle are reversed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR 1.136(a).

REVERSED

RONALD H. SMITH
Administrative Patent Judge

WILLIAM F. SMITH
Administrative Patent Judge

TEDDY S. GRON
Administrative Patent Judge

BOARD OF PATENT APPEALS AND INTERFERENCES

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APPENDIX--CLAIMS ON APPEAL

6. A method of preparing a cell-free antigenic solution useful in immunizing horses against S. zooepidemicus bacteria, the method comprising the steps of :

(a) growing S. zooepidemicus bacteria under growth inducing conditions;

(b) adding mutanolysin enzyme to the bacteria of step (a);

(c) incubating the bacteria of step (b) under conditions such that M-like protein becomes available for detergent extraction without deleterious effect on the M-protein;

(d) adding an anionic detergent to the product of step (c) to extract immunogenic M-like protein into a supernate;

(e) separating the soluble extracted M-like protein supernate from bacterial cells and cell debris; and

(f) sterilizing the soluble M-like protein supernate product of step (e).